AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method for treating a protein crystal with a solution containing a solvent and one or more molecule species in the solvent, ~~wherein the molecules have a molecular weight of < 500 Da,~~ comprising the following steps:

   - fixing the protein crystal on a holding device, without being embedded in a liquid environment; [[and]]
   - generating a gas stream of defined composition around the crystal; and
   - applying microdrops of ~~the~~ a solution onto the crystal, wherein the solution contains a solvent and one or more molecule species in the solvent, wherein the molecule species bind to the protein in the protein crystal as ligands and have a molecular weight of < 500 Da.

2. (Currently amended) The method for treating a protein crystal according to claim 1, wherein the molecules contained in the solution have a molecular weight of < 200 Da.

3. (Currently amended) The method for treating a protein crystal according to claim 1, wherein the molecules contained in the solution have a molecular weight of < 100 Da.

4. Cancelled.

5. (Currently amended) The method for treating a protein crystal according to claim [[4]] 1, wherein the molecules contained in the solution bind to the proteins in the protein crystal as ligands~~, preferably~~ with an affinity between 10^{-3} and 10^{-4} M.

6. (Currently amended) The method for treating a protein crystal according to claim 1, wherein the molecules contained in the solution or the molecules of at least one molecule species contained in the solution have at least one electron-rich or anomalous dispersion center, preferably a heavy(metal) atom.

7. Cancelled.

8. Cancelled.

9. (Currently amended) The method according to claim [[8]] 1, wherein the gas stream consists of an air stream with controlled air humidity.

10. (Currently amended) The method according to claim [[8]] 1, wherein the gas stream is regulated during the drip-on procedure.

11. (Previously presented) The method according to claim 9, wherein the air humidity of the gas stream and the frequency, at which the drops are dripped onto the crystal by means of the micro dosage system, are synchronized during the drip-on procedure in such a way that the crystal is strained as little as possible and, in particular, that the volume of the crystal alters by no more than 20%, in particular by no more than 10%.

12. (Currently amended) The method according to ~~claim 8~~ claim 1, wherein the gas stream comprises a solubilizer at a controlled concentration for a substance to be applied onto the crystal.

13. (Previously presented) The method according to claim 1, wherein the volume of the microdrops is smaller than the volume of the crystal.

14. (Previously presented) The method according to claim 13, wherein the microdrops of the solution have a volume of between 1 nl and 100 pl, preferably between 100 pl and 20 pl, and also preferably between 20 pl and 4 pl.

15. (Previously presented) The method according to claim 1, wherein the solution containing the molecule species and applied onto the crystal is an aqueous solution or a solution at least partially comprising organic solvents and, optionally, being heated up to more than 20°C.

16. (Previously presented) The method according to claim 15, wherein the solution containing the molecule species consists of or contains a volatile organic solvent.

17. (Previously presented) The method according to claim 16, wherein the solvent consists of or contains DMSO.

18. (Previously presented) The method according to claim 15, wherein the solvent containing the molecule species is or contains a preferably entirely volatile organic solvent, which boils at a temperature of below 100°C.

19. (Previously presented) The method according to claim 15, wherein the solvent contains DMSO, trifluoroethanol, acetone, chloroform, and/or methanol.

20. (Previously presented) The method according to claim 1, wherein the molecules contained in the solution to be applied onto the crystal are hardly water-soluble.

21. (Previously presented) The method according to claim 1, wherein the solution contains a cocktail of at least 3, more preferably at least 10, even more preferably at least 20, and most preferably at least 50 different molecule species.

22. (Previously presented) The method according to claim 1, wherein the solution contains at least one molecule species at a concentration of 10^{-1} to 10^{-3} M.

23. (Currently amended) The method according to claim 1, further comprising, before the ~~mixing~~ fixing and applying steps, a step of identifying fragments that potentially bind to a target structure using a spectroscopic method or an in silico docking method.

24. (Previously presented) The method according to claim 1, wherein the gas stream contains one or more substances, which contains one or more ligands and/or inhibitors.

25. (Previously presented) A method for determining a crystallographic structure of a complex, comprising (a) conducting the method steps according to claim 1, (b) irradiating the crystal with X-ray or synchrotron radiation, and (c) recording the diffraction image of the crystal.

26. (Previously presented) The method for determining a crystallographic structure according to claim 25, further comprising (d) calculating an electron density map using the phase information and the intensity of the reflexes in the diffraction image and determining the binding site and positioning of the at least one bound molecule species.

27. (Previously presented) The method according to claim 26, wherein the phase information is obtained using heavy metal atom derivatives ("isomorphous replacement"), "molecular replacement", or MAD (multiple anomalous scattering).

28. (Previously presented) The method for determining a crystallographic structure according to claim 26, wherein the binding site and positioning of the at least one bound molecule species in the structure is determined from the difference of electron densities of non-complexed and complexed structure by means of a electron density difference map.

29. (Previously presented) The method according to claim 25, wherein the irradiation is conducted with monochromatic X-ray radiation or with synchrotron radiation during the treatment of the crystal with the solution.

30. (Previously presented) A method for identifying molecules binding a crystallized protein, wherein (a) at least one molecule species is applied onto the crystal according to the method according to claim 1, (b) diffraction intensities are measured at intervals of variable length, and (c) said diffraction intensities measured at intervals are compared with respect to their time-dependent sequence.

31. (Previously presented) A method for identifying a ligand binding a target structure, comprising (a) determining the structure of at least one complex having at least two fragments according to the method according to claim 25, (b) determining at least one linker to a ligand, which is located between the at least two fragments, and (c) synthesizing a ligand containing the at least two fragments and the at least one linker.

32. (Previously presented) The method according to claim 1, wherein the method is conducted using a device for treating a crystal with a substance having a holder for fixing the crystal and at least one micro dosage system, which is arranged in relation to the holder in such a way that it can apply microdrops of the liquid onto the crystal fixed in the holder.

33. (Previously presented) The method according to claim 32, wherein the device used according to the method furthermore comprises a device capable of generating a defined environment around the crystal during the drip-on procedure.

34. (Previously presented) The method according to claim 32, wherein the device allows the generation of a defined environment by generating a gas stream of defined composition around the crystal.

35. (Previously presented) The method according to claim 34, wherein the holder is developed in such a way that the gas stream can be led through the holder in such a way that it is directed toward the crystal fixed in the holder.

36. (Previously presented) The method according to claim 1, wherein a device having a holder consisting of a carrier block for a holder capillary, which has a free support end for the crystal, is used.

37. (Previously presented) The method according to claim 36, wherein a device having a holder capillary consisting of a micropipette, in which a negative pressure can be generated in order to hold the crystal, is used.

38. (Previously presented) The method according to claim 36, wherein the carrier block of the holder of the device has an integrated gas channel having a mouth end, which is directed toward the support end of the holder capillary.

39. (Previously presented) The method according to claim 34, wherein a device is used, which has a gas mixing device capable of variably adjusting the composition of the gas stream.

40. (Previously presented) The method according to claim 39, wherein a device is used, in which the gas consists of air having a specific humidity content and the gas mixing device is capable of adjusting the air humidity.

41. (Previously presented) The method according to claim 34, wherein a device is used, which comprises a device for adding a solubilizer capable of adding to the gas stream a solubilizer for a substance to be introduced into the crystal structure of the crystal .

42. (Previously presented) The method according to claim 41, wherein a device is used, which comprises a concentration adjusting device for adjusting the concentration of the solubilizer.

43. (Previously presented) The method according to claim 34, wherein a device is used, which comprises a temperature regulating device capable of variably adjusting the temperature of the gas stream.

44. (Previously presented) The method according to claim 32, wherein a device is used, in which the micro dosage system is developed in such a way that it can generate microdrops of the liquid to be applied onto the crystal, which have a volume that is smaller than the volume of the crystal.

45. (Previously presented) The method according to claim 44, wherein a device is used, in which the micro dosage system is developed in such a way that it can generate microdrops having a volume of between 10 and 20 percent of the volume of the crystal and preferably between 5 and 10 percent of the volume of the crystal.

46. (Previously presented) The method according to claim 42, wherein the micro dosage system is developed in such a way that it can generate microdrops having a volume of between 1 nl and 100 pl, preferably between 100 pl and 20 pl, and also preferably between 20 pl and 4 pl.

47. (Previously presented) The method according to claim 1, wherein a device is used, in which the micro dosage system has a liquid supply system capable of supplying different liquids to be dripped onto the crystal, to a drop generating part of the micro dosage system in a time-dependently controlled manner.

48. (Previously presented) The method according to claim 47, wherein a device is used, in which the liquid supply system of the micro dosage system comprises an electrically controllable precision syringe and a duct system, with which the precision syringe can be connected, via electrically controllable valves, with different liquid supply containers and with the drop generating part of the micro dosage system in order to supply liquid for drop generation to the latter.

49. (Previously presented) The method according to claim 1, wherein a device is used, in which the micro dosage system is developed in such a way that it comprises a piezo pipette, which forms the drop generating part.

50. (Previously presented) The method according to claim 1, wherein the crystal is vapor-plated with solvent, in particular with organic solvent, by means of an evaporator.

51. (Currently amended) A method for X-ray crystallographic structure determination at high throughput, comprising (a) holding one or more crystals ready~~, preferably~~ in a freely mounted manner, (b) applying microdrops of a solution containing ~~at least one ligand~~ one or more molecule species wherein the molecule species have a molecular weight of less than 500 Daltons onto the preferably freely mounted crystals, (c) storing the crystals treated according to step (b), and (d) examining the crystals X-ray crystallographically.

52. (Currently amended) The method of Claim 23, wherein the spectroscopic method is NMR spectroscopy or ~~sufae~~ surface plasmon resonance spectroscopy.